Experimental coronary dilatation

Peter C. Block, M.D.

Boston, Massachusetts

Percutaneous coronary transluminal angioplasty has had increasing clinical application in patients with focal stenotic noncalcific coronary artery stenoses. The effects of coronary angioplasty have been evaluated in detail angiographically and a sequence of angiographic changes occurs with time in the immediate period after angioplasty and follow-up studies. Immediately following angioplasty the dilated area has a slightly "shaggy" endothelial appearance. In some cases there is not much improvement in lumen size seen angiographically. If the procedure is successful, lumen size is usually improved by at least 20% to 30% and in many cases to 70% or 80%. The irregular endothelial appearance seen angiographically in immediate postangioplasty angiograms is most prominent in femoral angioplasty sites, but is also seen after coronary angioplasty. In 6-month follow-up angiograms, "remodeling" of the dilated area is seen with smoothing of the inner surface of the artery. Frequently, there is improvement in lumen size compared to immediate postangioplasty angiograms. This angiographic appearance of remodeling implies that active changes have occurred within the vessel wall in the area of angioplasty. Remodeling of the medial/intimal surface may provide a larger, smoother lumen in the area that was previously stenotic.

Experimental angioplasty studies have been used to evaluate the pathophysiologic changes that occur immediately and following transluminal angioplasty. Attempts have been made to correlate pathologic changes seen in experimental models with the angiographic appearance seen in human angioplasty experience. Studies of experimental angioplasty have been performed at autopsy in human coronary arteries with coronary atherosclerosis, in normal canine coronary arteries, and in a "model" of atherosclerosis using rabbits fed a 2% cholesterol atherogenic diet.

Human autopsy studies

Studies of human hearts at autopsy within 24 hours of death have shown that most atherosclerotic stenoses can be dilated with the coronary angioplasty technique. However, in some instances extremely high intraballoon pressures are necessary to dilate the stenotic artery. When intraballoon pressures of more than 6 to 7 atmospheres of pressure are used, rupture of the artery or displacement of atheromatous material through the wall of the artery can occur.

In situations where the usual intraballoon "working" pressures of 4 to 6 atmospheres are used, coronary dilatation occurs if the lesion is noncalcified and not extensively fibrotic. The angiographic appearance of human coronary arteries at autopsy after dilatation shows improvement of the lumen size in almost all instances when the coronary dilatation catheter can be inflated with these pressures. Coronary artery dissection is rarely seen angiographically. Pathologically there is almost uniformly splitting of the atheromatous plaque with curvilinear splits of superficial sections of the fibrous cap overlying the atheromatous material. There is little evidence of atheromatous compression in these studies. These data are subject to the criticism that the coronary angioplasty is performed in nonviable hearts, and the validity of the findings has been questioned since nonviable tissue might be more prone to dissection and splitting than viable tissue.

Normal canine coronaries

Normal canine coronary arteries have been studied by electron microscopy to evaluate the effect of balloon angioplasty in an artery where the size of the dilated balloon and artery are approximately the same. Scanning electron microscopy of the area that underwent transluminal angioplasty shows extensive desquamation of endothelial elements with exposure of subendothelial microfibrils. Platelet deposition in the area of exposed microfibrils is extensive and occurs within 10 minutes after dilatation of the angioplasty balloon. Deposition of an occlusive platelet thrombus is probably minimized by maintenance of intracoronary flow. Within 24 to 48 hours the carpet of platelets overlying the exposed subendothelial microfibrils begins to metamorphose and produces a nonthrombogenic surface. Such changes are characteristic of any injury to endothelium. Endothelium is particularly prone to even minor injury, and exposure of subendothelial microfibrils and platelet deposition is a normal response to such injury. The implication of these studies is that maintenance of coronary flow is important after transluminal angioplasty to minimize platelet-thrombus formation. The effects of antiplatelet agents and long-term effects of anticoagulation and antiplatelet agents remain to be clarified.

Atherosclerotic rabbit model

To test the effects of transluminal angioplasty in an atherosclerotic animal model, endothelial debridement was carried out in rabbits fed a 2% cholesterol diet. The aorta and right iliac arteries were debrided using a Fogarty balloon, and within 6 to 10 weeks aortic and iliac atherosclerotic changes had occurred. The plaques seen in the vessel wall differ from human atherosclerotic plaques in that they are filled with foam cells rather than cholesterol clefts. There is considerable medial thickening and intimal proliferation. The model is not identical to human atherosclerosis, but may serve as a guide to the changes that occur in human subjects after coronary angioplasty.

Following transluminal angioplasty within the atherosclerotic vessel, endothelial desquamation similar to that seen in the coronary arteries of normal dogs is also seen in the rabbit model. In addition, shearing of superficial portions of the atherosclerotic plaque can be seen in areas of aortic atherosclerosis that had undergone transluminal angioplasty. If the size of the inflated transluminal angioplasty balloon and the atherosclerotic vessel are more disparate, as is seen in the iliac arteries of rabbits, splitting of the intima and even dissection of the artery can be produced. Evidence of dissection can be seen angiographically and histologically.

It appears that transluminal angioplasty produces the following changes immediately:

1. In arterial segments where the size of the atherosclerotic vessel and the size of the inflated angioplasty balloon are approximately equal, endothelial desquamation and shearing of superficial portions of atherosclerotic plaques occur.
2. In areas where the size of the inflated transluminal angioplasty balloon and atherosclerotic vessel are more disparate, splitting of the atheromatous plaque and local injury occur.
3. Sequential changes in the 2 weeks following transluminal angioplasty in the rabbit atherosclerotic model show the following:
   a. Some segments of artery have a persistent increase in lumen size without evidence of intimal splitting or disruption of the atheromatous plaque, presumably due to atheromatous compression.
   b. Endothelial splitting produces a fibrotic response within the first 2 weeks after transluminal angioplasty. Healing and fibrosis retract the intima and further enlarge the lumen in areas of atherosclerotic splitting.
   c. Areas of artery that had developed true dissections show endothelialization of the false channel with a "double-barrel" artery.

It is postulated that percutaneous transluminal coronary angioplasty probably produces a site of focal injury in the area of atherosclerotic narrowing. Superficial splits of the fibrous material overlying the atheromatous plaque occur at the time of balloon dilatation. This accounts for the irregular "shaggy" angiographic appearance seen so commonly in angiograms done immediately after the angioplasty procedure. There is probably some compression or movement of atheromatous material into the vessel wall and along planes of cleavage. Some atheromatous debris is almost certainly released into the circulation along with elements of endothelial cells. Embolization of this material has not been important clinically. Remodeling of the area of stenosis after angioplasty prob-

ably occurs due to the release of atheromatous debris in the circulation and to degradation of atheromatous material that has been compressed along planes of cleavage in the vessel wall. The atheromatous plaque is relatively metabolically inert. Release of some of its contents into the circulation and forcing of some of its contents into the vessel wall may produce an inflammatory response to the injury that may allow metabolic degradation of the atheroma. This degradation of atheromatous plaque material in time may account for the remodeling seen angiographically and may result in further enlargement of lumen size as is seen in follow-up angiograms at 6 weeks after percutaneous transluminal coronary angioplasty.